```
GAGCTCGGAT CCACTACTCG ACCCACGCGT CCGGCCAGGA CCTCTGTGAA CCGGTCGGGG   60

CGGGGGCCGC CTGGCCGGGA GTCTGCTCGG CGGTGGGTGG CCGAGGAAGG GAGAGAACGA  120

TCGCGGAGCA GGGCGCCCGA ACTCCGGGCG CCGCGCC ATG CGC CGG GCC AGC CGA  175
                                            Met Arg Arg Ala Ser Arg
                                             1                   5

GAC TAC GGC AAG TAC CTG CGC AGC TCG GAG GAG ATG GGC AGC GGC CCC  223
Asp Tyr Gly Lys Tyr Leu Arg Ser Ser Glu Glu Met Gly Ser Gly Pro
                10              15                        20

GGC GTC CCA CAC GAG GGT CCG CTG CAC CCC GCG CCT TCT GCA CCG GCT  271
Gly Val Pro His Glu Gly Pro Leu His Pro Ala Pro Ser Ala Pro Ala
                25              30                        35

CCG GCG CCG CCA CCC GCC GCC TCC CGC TCC ATG TTC CTG GCC CTC CTG  319
Pro Ala Pro Pro Pro Ala Ala Ser Arg Ser Met Phe Leu Ala Leu Leu
          40              45                        50
```

FIG.1A

GGG CTG GGA CTG GGC CAG GTG GTC TGC AGC ATC GCT CTG TTC CTG TAC
Gly Leu Gly Leu Gly Gln Val Val Cys Ser Ile Ala Leu Phe Leu Tyr   367
55   60   65   70

TTT CGA GCG CAG ATG GAT CCT AAC AGA ATA TCA GAA GAC AGC ACT CAC
Phe Arg Ala Gln Met Asp Pro Asn Arg Ile Ser Glu Asp Ser Thr His   415
              75   80   85

TGC TTT TAT AGA ATC CTG AGA CTC CAT GAA AAC GCA GGT TTG CAG GAC
Cys Phe Tyr Arg Ile Leu Arg Leu His Glu Asn Ala Gly Leu Gln Asp   463
              90   95   100

TCG ACT CTG GAG AGT GAA GAC ACA CTA CCT GAC TCC TGC AGG AGG ATG
Ser Thr Leu Glu Ser Glu Asp Thr Leu Pro Asp Ser Cys Arg Arg Met   511
              105   110   115

AAA CAA GCC TTT CAG GGG GCC GTG CAG AAG GAA CTG CAA CAC ATT GTG
Lys Gln Ala Phe Gln Gly Ala Val Gln Lys Glu Leu Gln His Ile Val   559
              120   125   130

FIG.1B

```
GGG  CCA  CAG  CGC  TTC  TCA  GGA  GCT  CCA  GCT  ATG  ATG  GAA  GGC  TCA  TGG    607
Gly  Pro  Gln  Arg  Phe  Ser  Gly  Ala  Pro  Ala  Met  Met  Glu  Gly  Ser  Trp
     135            140                 145                           150

TTG  GAT  GTG  GCC  CAG  CGA  GGC  AAG  CCT  GAG  GCC  CAG  CCA  TTT  GCA  CAC    655
Leu  Asp  Val  Ala  Gln  Arg  Gly  Lys  Pro  Glu  Ala  Gln  Pro  Phe  Ala  His
               155                 160                      165

CTC  ACC  ATC  AAT  GCT  GCC  AGC  ATC  CCA  TCG  GGT  TCC  CAT  AAA  GTC  ACT    703
Leu  Thr  Ile  Asn  Ala  Ala  Ser  Ile  Pro  Ser  Gly  Ser  His  Lys  Val  Thr
          170                      175                           180

CTG  TCC  TCT  TGG  TAC  CAC  GAT  CGA  GGC  TGG  GCC  AAG  ATC  TCT  AAC  ATG    751
Leu  Ser  Ser  Trp  Tyr  His  Asp  Arg  Gly  Trp  Ala  Lys  Ile  Ser  Asn  Met
                         185                      190                      195
```

FIG.1C

ACG TTA AGC AAC GGA AAA CTA AGG GTT AAC CAA GAT GGC TTC TAT TAC   799
Thr Leu Ser Asn Gly Lys Leu Arg Val Asn Gln Asp Gly Phe Tyr Tyr
        200   205   210

CTG TAC GCC AAC ATT TGC TTT CGG CAT CAT GAA ACA TCG GGA AGC GTA   847
Leu Tyr Ala Asn Ile Cys Phe Arg His His Glu Thr Ser Gly Ser Val
        215   220   225   230

CCT ACA GAC TAT CTT CAG CTG ATG GTG TAT GTC GTT AAA ACC AGC ATC   895
Pro Thr Asp Tyr Leu Gln Leu Met Val Tyr Val Val Lys Thr Ser Ile
                235   240   245

AAA ATC CCA AGT TCT CAT AAC CTG ATG AAA GGA GGG AGC ACG AAA AAC   943
Lys Ile Pro Ser Ser His Asn Leu Met Lys Gly Gly Ser Thr Lys Asn
        250   255   260

TGG TCG GGC AAT TCT GAA TTC CAC TTT TAT TCC ATA AAT GTT GGG GGA   991
Trp Ser Gly Asn Ser Glu Phe His Phe Tyr Ser Ile Asn Val Gly Gly
        265   270   275

FIG.1D

TTT TTC AAG CTC CGA GCT GGT GAA GAA ATT AGC ATT CAG GTG TCC AAC   1039
Phe Phe Lys Leu Arg Ala Gly Glu Glu Ile Ser Ile Gln Val Ser <u>Asn</u>
     280   285   290

CCT TCC CTG CTG GAT CCG GAT CAA GAT GCG ACG TAC TTT GGG GCT TTC   1087
Pro Ser Leu Leu Asp Pro Asp Gln Asp Ala Thr Tyr Phe Gly Ala Phe
     295   300   305   310

AAA GTT CAG GAC ATA GAC T GAGACTCATT TCGTGGAACA TTAGCATGGA   1136
Lys Val Gln Asp Ile Asp
              315

TGTCCTAGAT GTTTGGAAAC TTCTTAAAAA ATGGATGATG TCTATACATG TGTAAGACTA   1196

CTAAGAGACA TGGCCCACGG TGTATGAAAC TCACAGCCCT CTCTCTTGAG CCTGTACAGG   1256

TTGTGTATAT GTAAAGTCCA TAGGTGATGT TAGATTCATG GTGATTACAC AACGGTTTTA   1316

FIG.1E

```
CAATTTTGTA ATGATTTCCT AGAATTGAAC CAGATTGGGA GAGGTATTCC GATGCTTATG   1376

AAAAACTTAC ACGTGAGCTA TGGAAGGGGG TCACAGTCTC TGGGTCTAAC CCCTGGACAT   1436

GTGCCACTGA GAACCTTGAA ATTAAGAGGA TGCCATGTCA TTGCAAAGAA ATGATAGTGT   1496

GAAGGGTTAA GTTCTTTTGA ATTGTTACAT TGCGCTGGGA CCTGCAAATA AGTTCTTTTT   1556

TTCTAATGAG GAGAGAAAAA TATATGTATT TTTATATAAT GTCTAAAGTT ATATTTCAGG   1616

TGTAATGTTT TCTGTGCAAA GTTTTGTAAA TTATATTTGT GCTATAGTAT TTGATTCAAA   1676

ATATTTAAAA ATGTCTCACT GTTGACATAT TTAATGTTTT AAATGTACAG ATGTATTTAA   1736

CTGGTGCACT TTGTAATTCC CCTGAAGGTA CTCGTAGCTA AGGGGGCAGA ATACTGTTTC   1796

TGGTGACCAC ATGTAGTTTA TTTCTTTATT CTTTTTAACT TAATAGAGTC TTCAGACTTG   1856
```

FIG.1F

```
TCAAAACTAT GCAAGCAAAA TAAATAAATA AAAATAAAAT GAATACCTTG AATAATAAGT   1916

AGGATGTTGG TCACCAGGTG CCTTTCAAAT TTAGAAGCTA ATTGACTTTA GGAGCTGACA   1976

TAGCCAAAAA GGATACATAA TAGGCTACTG AAATCTGTCA GGAGTATTTA TGCAATTATT   2036

GAACAGGTGT CTTTTTTTAC AAGAGCTACA AATTGTAAAT TTTGTTTCTT TTTTTTCCCA   2096

TAGAAAATGT ACTATAGTTT ATCAGCCAAA AAACAATCCA CTTTTTAATT TAGTGAAAGT   2156

TATTTTATTA TACTGTACAA TAAAAGCATT GTCTCTGAAT GTTAATTTTT TGGTACAAAA   2216

AATAAATTTG TACGAAAACC TGAAAAAAAA AAAAAAAGGG CGGCCGCTCT              2276

AGAGGGCCCT ATTCTATAG                                              2295
```
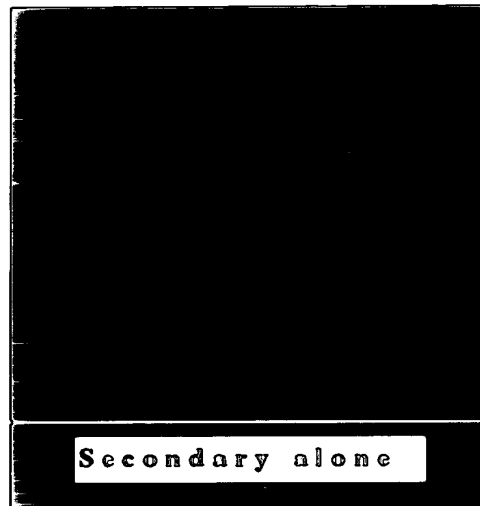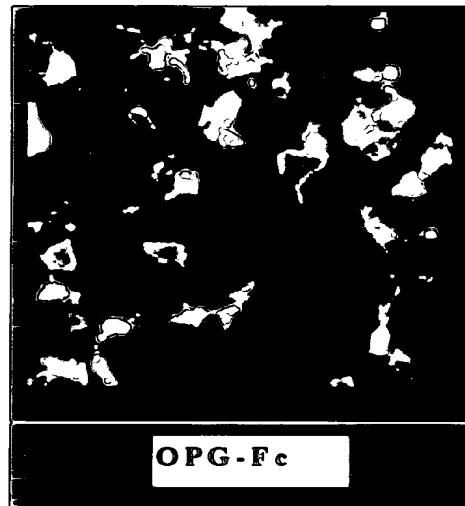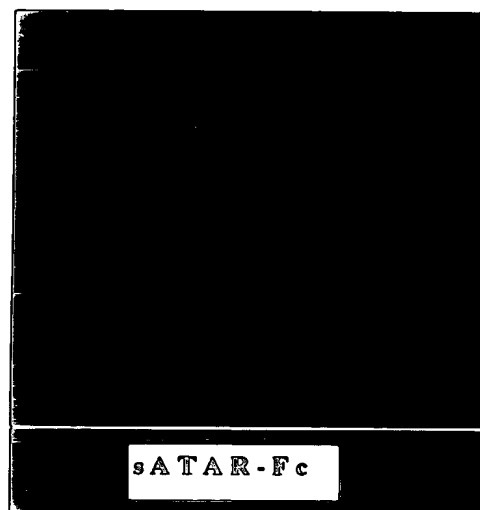
FIG.1G

FIG.2A

Secondary alone

FIG.2B

OPG-Fc

FIG.2C

sATAR-Fc
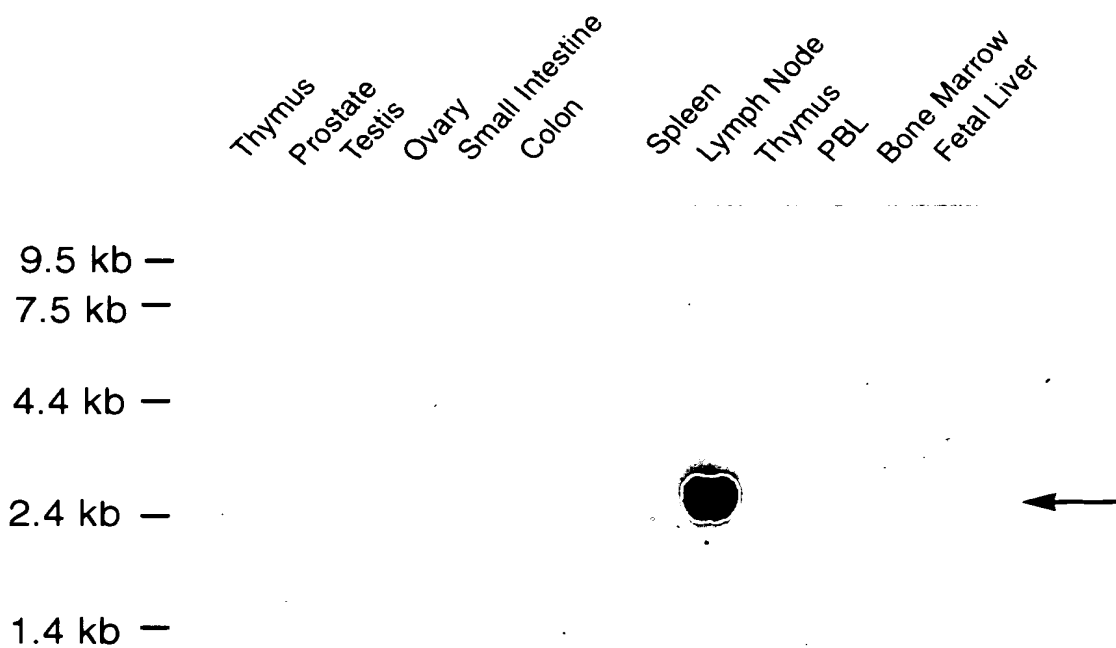
FIG.3

```
                    10                  30                  50
AAGCTTGGTACCGAGCTCGGATCCACTACTCGACCCACGGTCCGCGCCCCAGGAGCC

            70                  90                  110
AAAGCCGGGCTCCAAGTCGGCGCCCCCGAGGCTCCGAGCTCCGCCAGCCTCCGGAGTTGGC

            130                 150                 170
CGCAGACAAGAGGGGAGCGGGGAGGAGGAGAGCTCCGAAGCCGAGAGGGCCGAG

            190                 210                 230
CGCCATGCGCCGGCCAGCAGAGACTACACCAAGTACCTGCTGCGTCGGAGGAGATGGG
     M  R  R  A  S  R  D  Y  T  K  Y  L  R  G  S  E  E  M  G

            250                 270                 290
CGGCGGCCCCGGAGCCCCCACGAGGGCCCCCTGCACGCCCCGCCCCCGCCTGCGCCGCCA
 G  G  P  G  A  P  H  E  G  P  L  H  A  P  P  P  P  P  A  P  H

            310                 330                 350
CCAGCCCCCGCCGCTCCCGCTCCATGTTCGTGGCCCTCCTGGGGGCTGGGGCTGGGCCA
 Q  P  P  A  A  S  R  S  M  F  V  A  L  L  G  L  G  L  G  Q

            370                 390                 410
GGTTGTCTGCAGCCGTCGCCCCTGTTCTTCTATTTCAGAGCCGCAGATGGATCCTAATAGAAT
 V  V  C  S  V  A  L  F  F  Y  F  R  A  Q  M  D  P  N  R  I
```

FIG.4A

430   450   470
ATCAGAAGAGATGGCACTCACTGCATTTATAGAATTTTGAGACTCCATGAAAATGCAGATTT
S   E   D   G   T   H   C   I   Y   R   I   L   R   L   H   E   N   A   D   F

490   510   530
TCAAGACACAACTCTGGAGAGTCAAGATACAAAATTAATACCTGATTCATGTAGGAGAAT
Q   D   T   T   L   E   S   Q   D   T   K   L   I   P   D   S   C   R   R   I

550   570   590
TAAACAGGCCTTTCAAGGAGCTGTGCAAAAGGAATTACAACATATCGTTGGATCACAGCA
K   Q   A   F   Q   G   A   V   Q   K   E   L   Q   H   I   V   G   S   Q   H

610   630   650
CATCAGAGCAGAGAAAGCCATGGTGGATGGCTCATGGTTAGATCTGGCCAAGAGGAGCAA
I   R   A   E   K   A   M   V   D   G   S   W   L   D   L   A   K   R   S   K

670   690   710
GCTTGAAGCTCAGCCTTTTGCTCATCTCACTATTAATGCCACCGACATCCCATCTGGTTC
L   E   A   Q   P   F   A   H   L   T   I   N   A   T   D   I   P   S   G   S

730   750   770
CCATAAAGTGAGTCTGTCCTCTTGGTACCATGATCGGGGTTGGGCCAAGATCTCCAACAT
H   K   V   S   L   S   S   W   Y   H   D   R   G   W   A   K   I   S   N   M

FIG.4B

790   810   830

GACTTTTAGCAATGGAAAACTAATAGTTAATCAGGATGGCTTTTATTACCTGTATGCCAA
T F S N G K L I V N Q D G F Y Y L Y A N

850   870   890

CATTTGCTTTCGACATCATGAAACTTCAGGAGACCTAGCTACAGAGTATCTTCAACTAAT
I C F R H H E T S G D L A T E Y L Q L M

910   930   950

GGTGTACGTCACTAAAACCAGCATCAAAATCCCAAGTTCTCATACCCTGATGAAAGGAGG
V Y V T K T S I K I P S S H T L M K G G

970   990   1010

AAGCACCAAGTATTGGTCAGGGAATTCTGAATTCCATTTTTATTCCATAAACGTTGGTGG
S T K Y W S G N S E F H F Y S I N V G G

1030   1050   1070

ATTTTTTAAGTTACGGTCTGGAGAGGAAATCAGCATCGAGTCTCCAACCCCTCCTTACT
F F K L R S G E E I S I E V S N P S L L

1090   1110   1130

GGATCCGGATCAGGATGCAACATACTTTGGGGCTTTAAAGTTCGAGATATAGATTGAGC
D P D Q D A T Y F G A F K V R D I D

FIG.4C

```
      1150            1170            1190
CCCAGTTTTTGGAGTGTGTTATGTATTCCTGGATGTTTGGAAACATTTTTAAAACAAGCC

      1210            1230            1250
AAGAAAGATGTATATAGGTGTGTGAGACTACTAAGAGGCATGGCCCCAACGGTACACGAC

      1270            1290            1310
TCAGTATCCATGCTCCTTGACCTTGTAGAGAAACACGGCGTATTACAGCCAGTGGGAGATGT

      1330            1350            1370
TAGACTCATGGTGTGTTACACAATGGTTTTTAAATTTGTAATGAATTCCTAGAATTAAA

      1390            1410            1430
CCAGATTGGAGCAATTACGGGTTGACCTTATGAGAAACTGCATGTGGGCTATGGGGAGGGG
```

FIG.4D

1450
TTGGTCCCTGGTCATGTGCCCCTTCGCAGCTGAAGTGGAGAGGGTGTCATCTAGCGCAAT

1470

1490

1510
TGAAGGATCATCTGAAGGGGCAAATTCTTTTGAATTGTTACATCATGCTGGAACCTGCAA

1530

1550

1570
AAAATACTTTTTCTAATGAGGAGAGAAAATATATGTATTTTATATATCTAAAGTTA

1590

1610

1630
TATTTCAGATGTAATGTTTTCTTTGCAAAGTATTGTAAATTATATTGTGCTATAGTATT

1650

1670

1690
TGATTCAAAATATTTAAAAATGTCTTGTTGACATATTTAAATGTTTTAAATGTACAGA

1710

1730

1750
CATATTTAACTGGTGCACTTTGTAAATTCCCCTGGGGAAAACTTGCAGCTAAGGAGGGGAA

1770

1790

1810
AAAAATGTTGTTTCCTAATATCAAATGCAGTATATTTCTTCGTTCTTTTTAAGTTAATAG

1830

1850

FIG.4E

```
                                                               1910
                            1890
           1870
ATTTTTTCAGACTGTCAAGCCTGTGCAAAAAATTAAAATGGATGCCTTGAATAATAAG

                                                               1970
                            1950
           1930
CAGGATGTTGGCCACCAGGTGCCTTTCAAATTTAGAAACTAATTGACTTTAGAAAGCTGA

                                                               2030
                            2010
           1990
CATTGCCAAAAAGGATACATAATGGGCCACTGAAATCTGTCAAGAGTAGTTATATAATTG

                                                               2090
                            2070
           2050
TTGAACAGGTGTTTTCCACAAGTGCCGCAAATTGTACCTTTTTTTTTTTTCAAAATAG

                                                               2150
                            2130
           2110
AAAAGTTATTAGTGGTTTATCAGCAAAAAGTCCAATTTTAATTTAGTAAATGTTATCTT

                                                               2210
                            2190
           2170
ATACTGTACAATAAAAACATTGCCTTTGAATGTTAATTTTTTGGTACAAAATAAATTTA

                                                               2270
                            2250
           2230
TATGAAAAAAAAAAAAAAGGGGCCGCTCTAGAGGGCCCTATTCTATAG
```

FIG.4F

+ OPG Binding Protein only

● OPG Binding Protein+Murine OPG [22-401]-Fc 1000ng/ml

■ OPG Binding Protein+Murine OPG [22-401]-Fc 500ng/ml

◄ OPG Binding Protein+Murine OPG [22-401]-Fc 100ng/ml

✕ OPG Binding Protein+Murine OPG [22-401]-Fc 10ng/ml
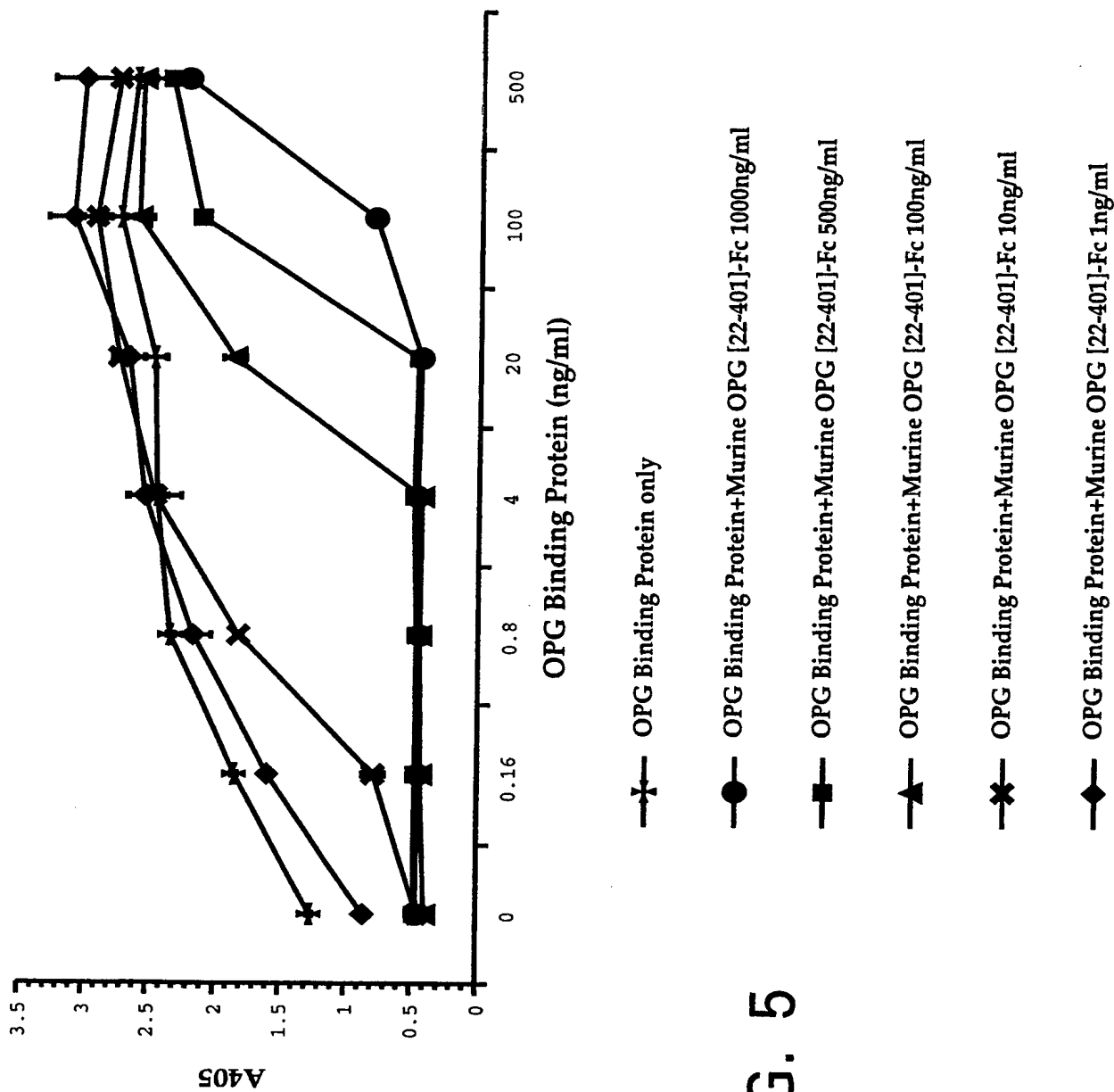
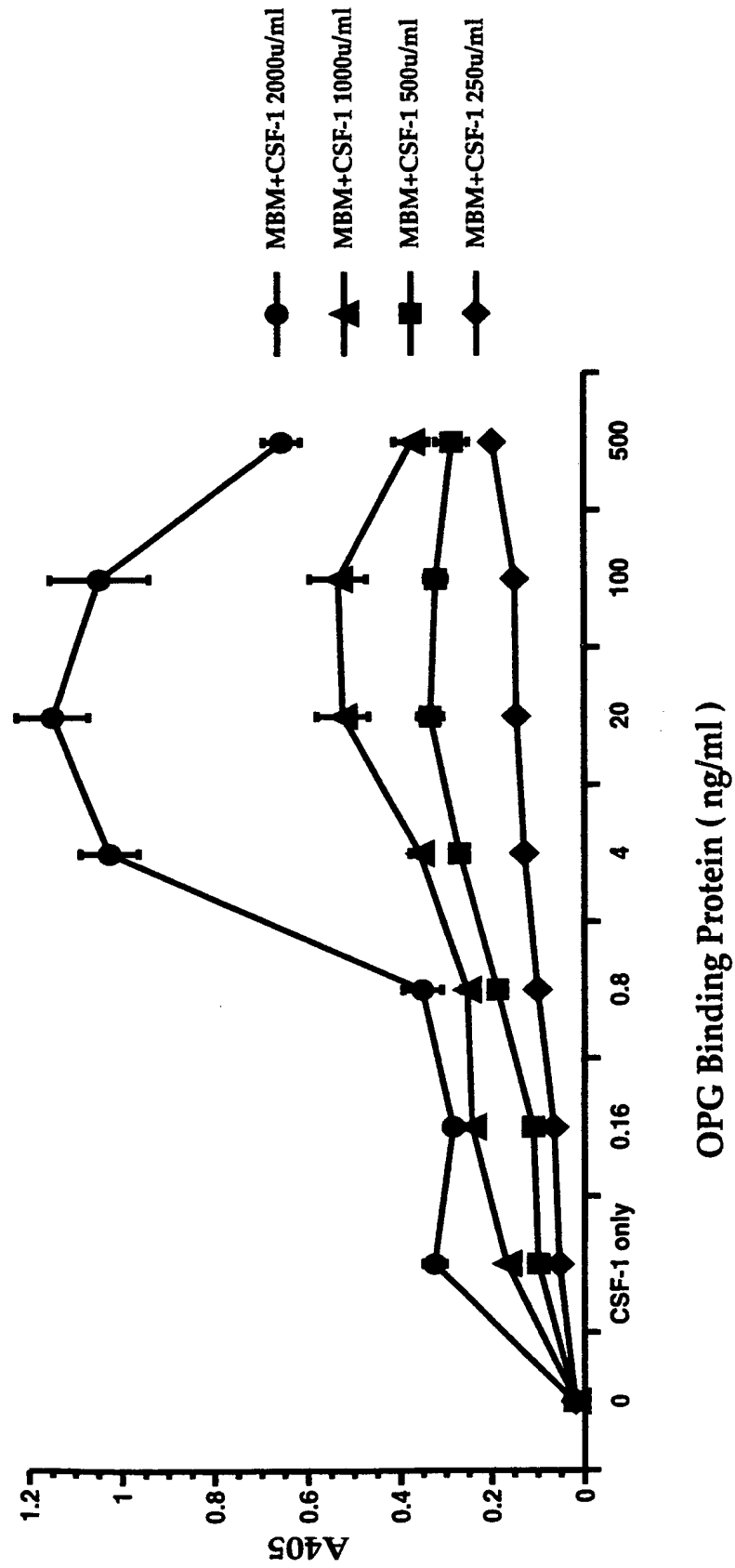◆ OPG Binding Protein+Murine OPG [22-401]-Fc 1ng/ml
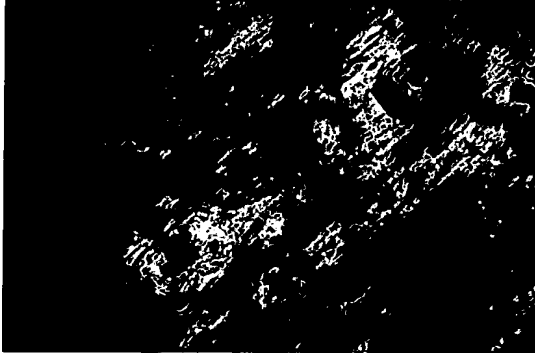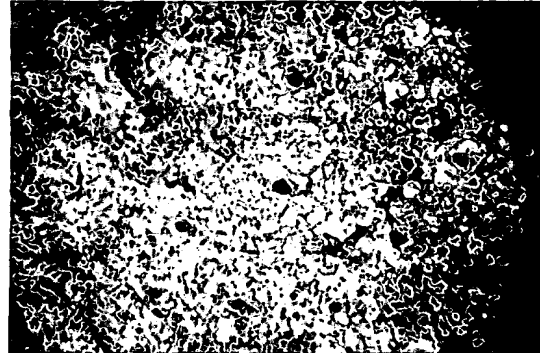
FIG. 5

FIG. 6

FIG.7A

Toluidine Blue Staining   TRAP staining

Bone Marrow Cells + M-CSF-1

FIG.7B

Toluidine Blue Staining   TRAP staining
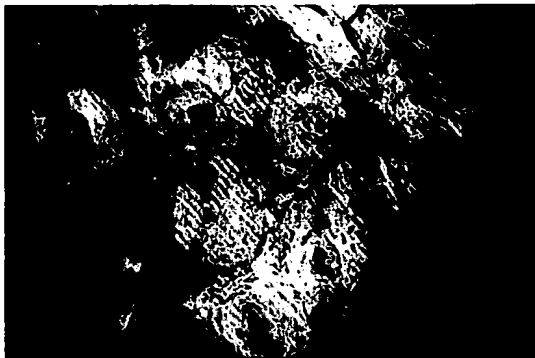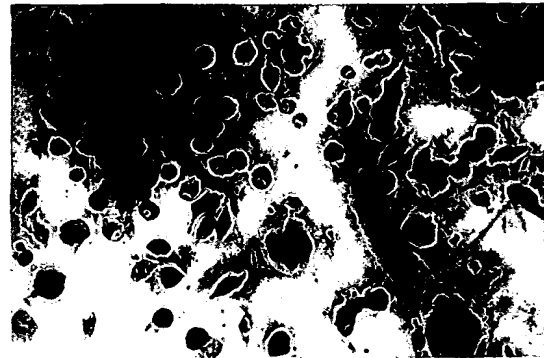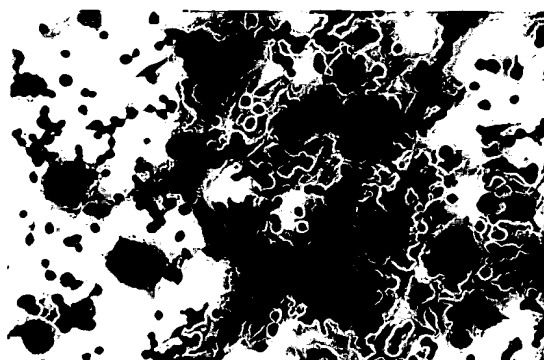

Bone Marrow Cells + OPG Binding Protein

FIG.7C

Toluidine Blue Staining   TRAP staining
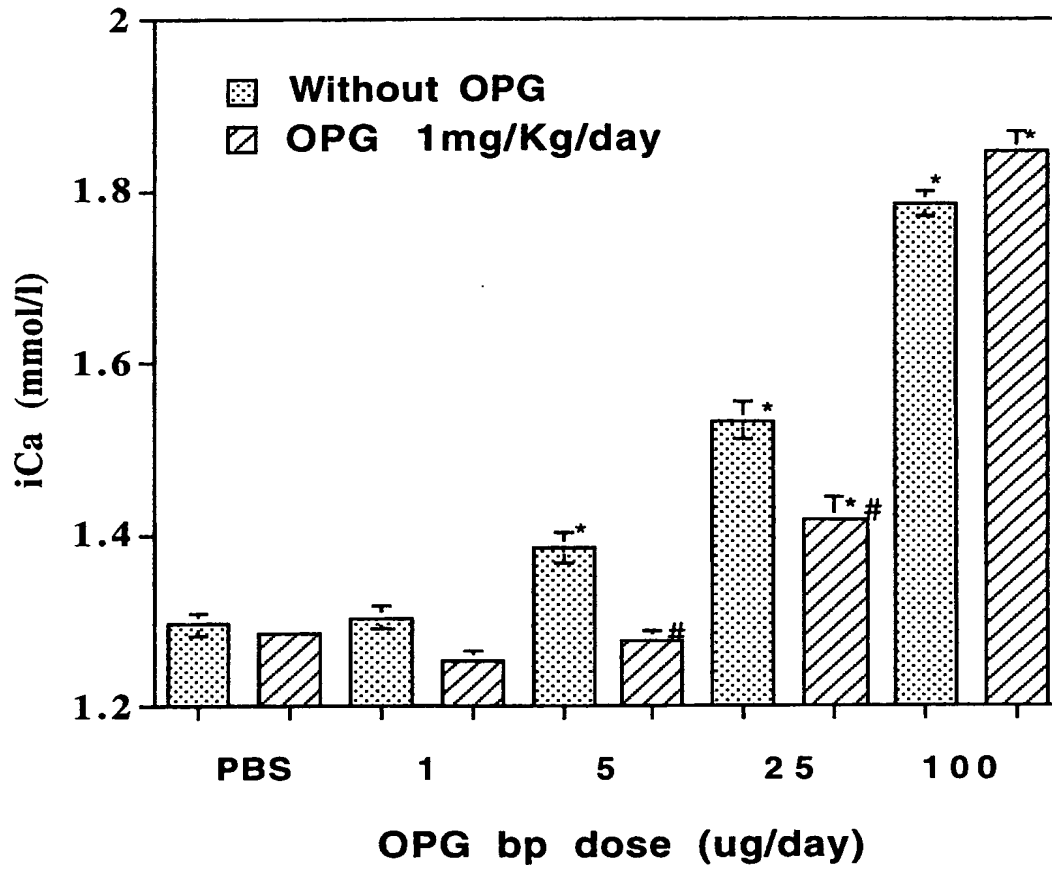

Bone Marrow Cells + M-CSF-1 +OPG Binding Protein

FIG. 8

PBS   **OPGbp 5ug/d**

FIG.9A   FIG.9B

OPGbp 25ug/d   **OPGbp100ug/d**

FIG.9C   FIG.9D

```
                    10              30              50
ACTCGACCCCACGGTCCGCCCGCCCCGCCGCCATGGACCCGCGCGCGCGGCGGCGCC
                                        M  D  P  R  A  R  R  R  R

                    70              90              110
GCCAGCTGCCCGGCCCGGCTGCTGGCGCTCTGCGTGCTGCTCGTTCCACTGCAGGTGACTC
Q  L  P  A  P  L  L  L  A  L  C  V  L  L  V  P  L  Q  V  T  L

                    130             150             170
TCCAGGTCACTCCTCCATGCACCCAGGAGAGGCATTATGAGCATCTCGGACGGTGTTGCA
Q  V  T  P  P  C  T  Q  E  R  H  Y  E  H  L  G  R  C  C  S

                    190             210             230
GCAGATGCGAACCAGGAAAGTACCTGTCCCTCTAAGTGCACTCCTACCTCCGACAGTGTGT
R  C  E  P  G  K  Y  L  S  S  K  C  T  P  T  S  D  S  V  C

                    250             270             290
GTCTGCCCGTGTGGCCCCGATGAGTACTTGGACACCTGGAATGAAGAAGATAAATGCTTGC
L  P  C  G  P  D  E  Y  L  D  T  W  N  E  E  D  K  C  L  L

                    310             330             350
TGCATAAAGTCTGTGATGCAGGCAAGGCCCTGGTGGCGGTGGATCCTGGCAACCACACGG
H  K  V  C  D  A  G  K  A  L  V  A  V  D  P  P  G  N  H  T  A
```

FIG.10A

```
     370                   390                   410
CCCCGGCGTCGGCTGTGCTTGCACGGCTGGCTACCACTGAACTCAGACTGCGAGTGCTGCC
 P   R   R   C   A   C   T   A   G   Y   H   W   N   S   D   C   E   C   C   R

                           430                   450                   470
GCAGGAACACGGAGTGTGCACCTGGCTTCGGAGCTTCAGCATCCCCTTGCAGCTCAACAAGG
 R   N   T   E   C   A   P   G   F   G   A   Q   H   P   L   Q   L   N   K   D

                           490                   510                   530
ATACGGTGGTGCACACCCTGCCTCCCGGGCTTCCTTCTCAGATGTCTTTCGTCCACAGACA
 T   V   C   T   P   C   L   L   G   F   F   S   D   V   F   S   S   T   D   K

                           550                   570                   590
AATGCAAACCTTGGACCAACTGCACCCTCCTTGGAAAGCTAGAAGCACACCAGGGACAA
 C   K   P   W   T   N   C   T   L   L   G   K   L   E   A   H   Q   G   T   T

                           610                   630                   650
CGGAATCAGATGTGGTGGTCTGCAGCTCTTCCATGACACTGAGGAGGAGACCACCCAAGGAGGCCC
 E   S   D   V   V   C   S   S   S   M   T   L   R   R   P   P   K   E   A   Q
```

FIG.10B

```
                670              690              710
AGGCTTACCTGCCCAGTCTCATCGTTCTGCTCCTTCCATCTCTGTGTGGTAGTAGTGGCTG
  A  Y  L  P  S  L  I  V  L  L  L  F  I  S  V  V  V  V  A  A
                730              750              770
CCATCATCTTCGGCGTTACTACAGAAGGAGGAAAGCGCTGACAGCTAATTTGTGGA
  I  I  F  G  V  Y  Y  R  K  G  G  K  A  L  T  A  N  L  W  N
                790              810              830
ATTGGGTCAATGATGCTTGCAGTAGTCTAAGTGGAAATAAGGAGTCCTCAGGGACCGTT
  W  V  N  D  A  C  S  S  L  S  G  N  K  E  S  S  G  D  R  C
                850              870              890
GTGCTGGTTCCCACTCGGCAACCTCCAGTCAGCAAGAAGTGTGTGAAGTATCTTACTAA
  A  G  S  H  S  A  T  S  S  Q  Q  E  V  C  E  G  I  L  L  M
                910              930              950
TGACTCGGGAGGAGAAGATGGTTCCAGAAGACGGTGCTGGGCCTGTGTGTGTG
  T  R  E  E  K  M  V  P  E  D  G  A  G  V  C  G  P  V  C  A
                970              990              1010
CGGCAGGTGGGCCCTGGGCAGAAGTCAGAGATTCTAGGACGTTCACACTGGTCAGCGGAGG
  A  G  G  P  W  A  E  V  R  D  S  R  T  F  T  L  V  S  E  V
```

FIG.10C

1030   1050   1070
TTGAGACGCCAAGGAGACCTCTCGAGGAAGATTCCCACAGAGGATGAGTACACGGACCGGC
 E T Q G D L S R K I P T E D E Y T D R P

1090   1110   1130
CCTCGCAGCCTTCGACTGGTTCACTGCTCCTAATCCAGCAGGAAGCAAATCTATACCCC
 S Q P S T G S L L L I Q Q G S K S I P P

1150   1170   1190
CATTCCAGGAGCCCCTGGAAGTGGGGGAGAACGACAGTTTAAGCCAGTGTTTCACCGGGA
 F Q E P L E V G E N D S L S Q C F T G T

1210   1230   1250
CTGAAAGCACGGTGGATTCTGAGGGCTGTGACTTCACTGAGCCTCCGAGCAGAACTGACT
 E S T V D S E G C D F T E P P S R T D S

1270   1290   1310
CTATGCCCGTCCCCTGAAAAGCACCTGACAAAAGAAATAGAAGGTGACAGTTGCCTCC
 M P V S P E K H L T K E I E G D S C L P

1330   1350   1370
CCTGGGGTGGTCAGCTCCAACTCAACAGATGGCTACACAGGCAGTGGGAACACTCCTGGGG
 W V V S S N S T D G Y T G S G N T P G E

FIG.10D

```
              1390                   1410                   1430
AGGACCATGAACCCTTTCCAGGTCCCTGAAATGTGGACCATTGCCCCAGTGTGCCTACA
 D   H   E   P   F   P   G   S   L   K   C   G   P   L   P   Q   C   A   Y   S

              1450                   1470                   1490
GCATGGGCTTTCCCAGTGAAGCAGCCAGCAGCCATGGCAGAGGCGGGAGTACGGCCCCAGG
 M   G   F   P   S   E   A   A   A   S   M   A   E   A   G   V   R   P   Q   D

              1510                   1530                   1550
ACAGGGCTGATGAGAGGGGAGCCTCAGGGTCCGGGAGCTCCCCAGTGACCAGCCACCTG
 R   A   D   E   R   G   A   S   G   S   S   P   S   D   Q   P   P   A

              1570                   1590                   1610
CCTCTGGGAACGTGACTGGAAACAGTAACTCCACGTTCATCTCTAGCGGGCAGGTGATGA
 S   G   N   V   T   G   N   S   N   S   T   F   I   S   S   G   Q   V   M   N

              1630                   1650                   1670
ACTTCAAGGGTGACATCATCGTGGTGTATGTCAGCCAGACCTCGCAGGAGGGCCCGGGTT
 F   K   G   D   I   I   V   V   Y   V   S   Q   T   S   Q   E   G   P   G   S

              1690                   1710                   1730
CCGCAGAGCCCGAGTCGGAGCCCGTGGGCCGCCCTGTGCAGGAGGAGACGCTGGCACACA
 A   E   P   E   S   E   P   V   G   R   P   V   Q   E   E   T   L   A   H   R
```

FIG.10E

```
                1750              1770              1790
GAGACTCCTTTGCGGGCACCGGCCCGGCGCTTCCCGAGCGTCTGTGCCACCGGGGCTGGGC
 D   S   F   A   G   T   A   P   R   F   P   D   V   C   A   T   G   A   G   L
                1810              1830              1850
TGCAGGAGCAGGGGGCACCCCGGCAGAAGGACGGGACATCGCGGCGGTGCAGGAGCAGG
 Q   E   Q   G   A   P   R   Q   K   D   G   T   S   R   P   V   Q   E   Q   G
                1870              1890              1910
GTGGGGCGCAGACTTCACTCCATACCCAGGGGTCCGACAATGTGCAGAATGACCTCACC
 G   A   Q   T   S   L   H   T   Q   G   S   G   Q   C   A   E
                1930              1950              1970
TTCTCTGTCTGCCCTGGGGTGCAGGCACCAGTGCCTTTCCAAAACATGGTGTAGCTAGC
                1990              2010              2030
CACTGTGCACCTCCTCACTGGTGCTGGCAGGCTGCATGGTGATGGAGCCCACCTCTCACT
                2050              2070
TCCTCCAGTGCCCCTCTCCTCTGCCTCCTAC
```

FIG.10F

FIG. 11A

FIG. 11B

FIG. 11C
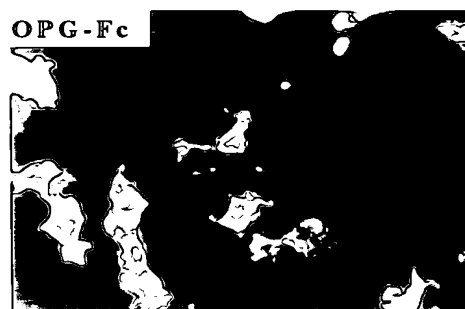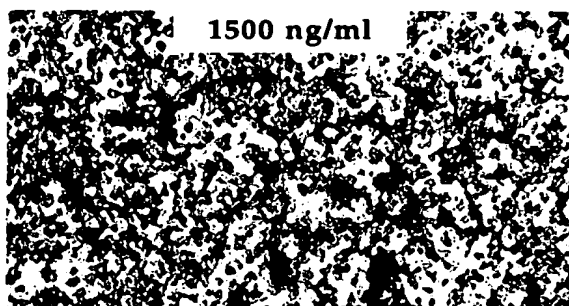
FIG.12A
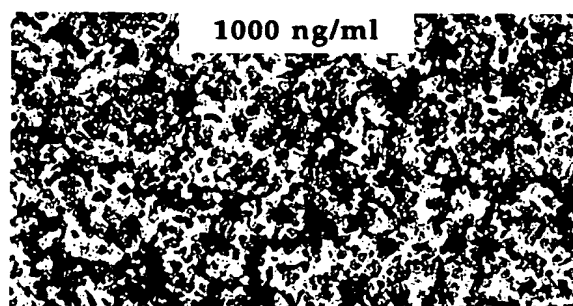
FIG.12B
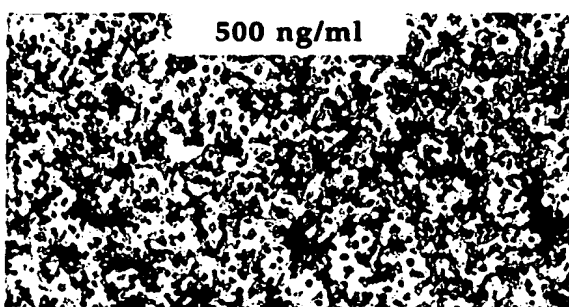
FIG.12C
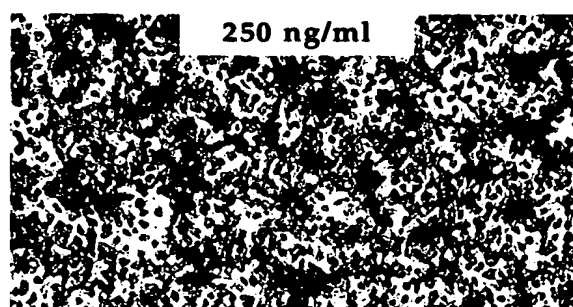
FIG.12D
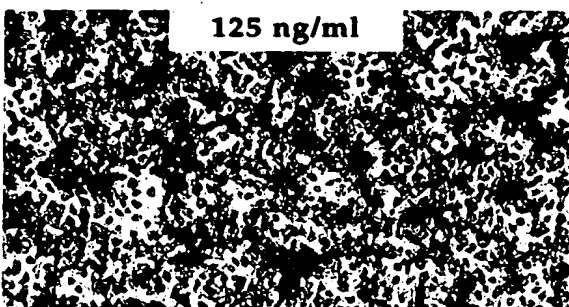
FIG.12E

FIG.12F

FIG.12G

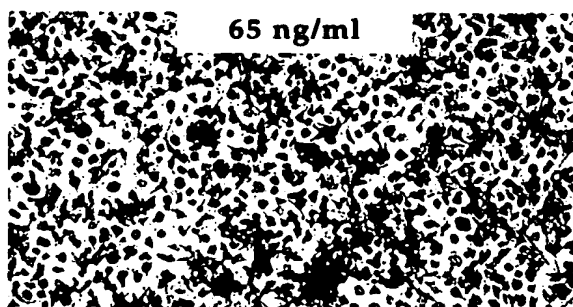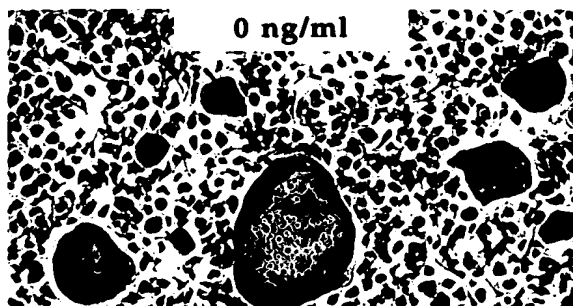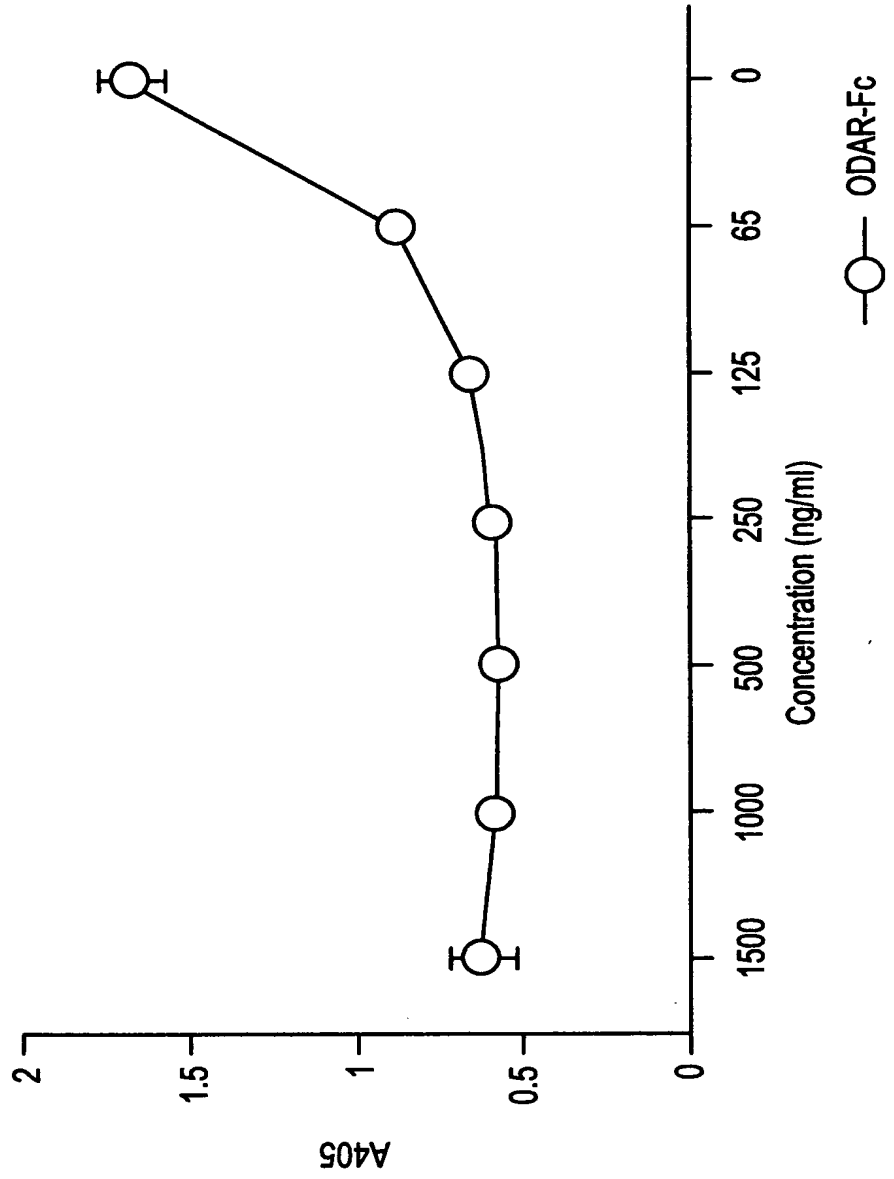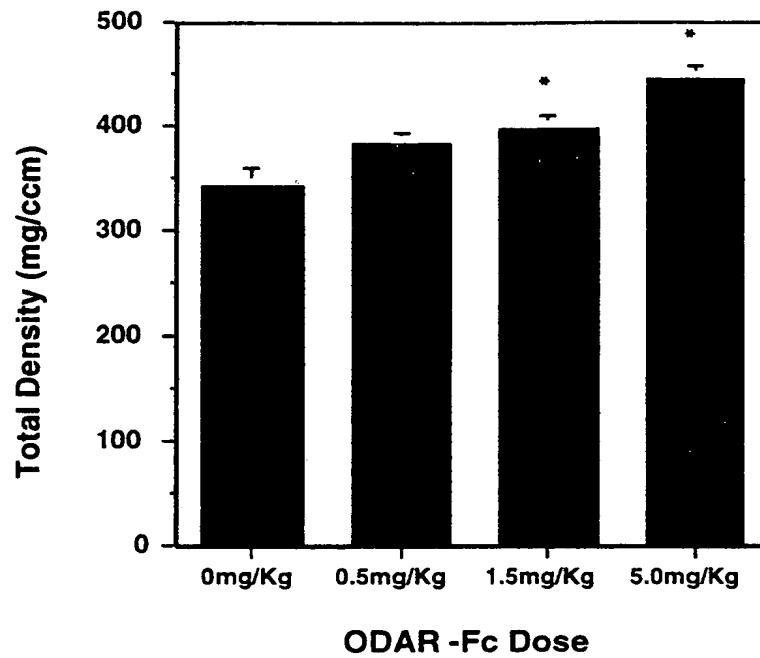# FIG. 12H

* Different to vehicle treated control p < 0.05.

FIG.13